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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,492	06/10/2002	Russell John Diefenbach	47-165	1732

7590 04/23/2003

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EXAMINER
SALIMI, ALI REZA

ART UNIT	PAPER NUMBER
1648	8

DATE MAILED: 04/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/031,492	Diefenbach et al
Examiner	**Art Unit**
A. R. SALMI	1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *6/10/02; 2/25/02* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-20* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *6*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *SEQUENCE LETTER*

DETAILED ACTION

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1648.

Response to Amendment

The receipt of preliminary amendment of 6/10/02, is acknowledged. Claims 1-20 are pending.

Claims 1-20 are pending.

Submitted Information Disclosure Statement (I.D.S) is noted.

Notice of draftsperson's patent drawing review (PTO 948) is enclosed.

Sequence Requirements

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. For example, see page 9.

Full compliance with the sequence rules is required in response to this Office Action. A complete response to this office action should include both compliance with the sequence rules and a response to the Office Action as set forth below. Failure to fully comply with **both** these requirements in the time period set forth in this office action will be held non-responsive.

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 USC § 112

Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP

§ 2172.01. The omitted elements are: the compound, the tegument protein, the type of virus, the motor protein, etc.. This affects the dependent claims.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: when to add, where to administer, how much, what to detect, when to detect, how to monitor the "prevention" of the virus transport, etc...

Claim 1 is vague and indefinite for recitation of "reducing", this is a relative term and is subject to varied interpretation. The said term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In addition, the intended meets and bounds of the "tegument protein" is not defined. The intended virus is not defined, and the intended "motor" protein is not defined. This affects the dependent claims.

Claim 4 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 4 does not appear to be further limiting claim 1. Claim 4 is directed to the same vague and indefinite limitations as recited in claim 1. The scope of claim 4 and 1 appear to be the same. Please clarify. In addition, claim 4 is confusing for recitation of

"capable of altering", the said term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. This affects the dependent claims.

Claims 5, 6, 15, 16 are vague and indefinite for recitation of "motor protein-like molecule", the intended compound is/are not defined. In addition, claims 5, 15 are vague and indefinite for recitation of "protein like molecule", what is a protein like molecule? Claim 6, 16 are further indefinite for recitation of "comprises a mimic of a cellular motor protein", the intended, "mimic protein" is/are not defined. This affects the dependent claims.

Claims 7, 17 are indefinite for recitation of "motor protein-like molecule is a mimic of kinesin or a part of kinesin", the intended metes and bounds of " mimic kinesin" or a part thereof is not defined.

Claims 8, 9, 18 are vague and indefinite for recitation of "tegument-like molecule", the intended "like molecule" is not defined. This affects the dependent claims.

Claim 10 is vague and indefinite for recitation of "molecule is a mimic of US11", the intended molecule(s) which "mimics" US11 is /are not defined.

Claim 11 is indefinite for recitation of "reduces" this is a relative terminology and is subject to varied interpretation.

Claim 12 is vague and indefinite, the intended "compound" is not defined. Is SDS intended? In addition, the claim is confusing for recitation of " a composition comprising", the composition comprising has to have more than one element, presently not even one of the element

has been defined. In addition, the claim is confusing for recitation of "capable of", it is not clear whether or not the intended "compound" actually prevents the binding or is only "capable", which may mean sometimes it does and sometimes it doesn't. Or it may mean the compound has a capacity to function as an antiviral which prevents binding, but whether or not it actually does prevent binding depends on many factors which would affect its "capability" as a viral inhibitor. Hence, the scope of "capable of" cannot be clearly deciphered. In addition, the intended "tegument" is not defined. This affects the dependent claims.

Claims 19 and 20 are vague and indefinite for recitation of "structural tegument-like molecule", what is the intended molecule, the metes and bounds of the "tegument-like" is not defined. In addition, claim 19 is vague and indefinite for recitation of "mimic of a viral tegument protein or a part of the tegument protein", the intended said protein(s) is/are not defined. Still further, in claim 19 the "cellular motor protein" is not defined. In addition, claim 20 is indefinite for recitation of "molecule is a mimic of US11", the intended molecule(s) which "mimics" US11 is /are not defined.

Claim Rejections - 35 USC § 112

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for only an *in vitro* method of screening compounds that would inhibit the anterograde axonal transport of nucleocapsid of Herpes Simplex Virus (HSV) tegument US11

protein via kinesin microtubule dependent protein by inhibiting the binding of HSV US11 protein to kinesin protein, does not reasonably provide enablement for any and all methods or products that would prevent or "reduce" transport of any and all neurotropic virus wherein the compound prevents the binding of any and all tegument protein of virus to any and all motor protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. At the onset Applicants are reminded that this field is considered to be highly unpredictable and absent adequate teaching one or ordinary skill in the art would be required to conduct large quantity of undue experimentations to enable the full scope of the claimed invention. The specification does not provide adequate teaching for all "compounds", teguments either mimic tegument or fragments thereof, motor proteins or mimic proteins within the broad scope of the claimed invention. The role of tegument are not yet well understood, they are not involved exclusively in viral transport, and viral transport is not exclusively via teguments either. Applicants' own disclosure is a testament to the unpredictability of the field. There are multiple ways for a virus to gain entry to a cell in general or a neuron cell in particular (see page 13 of the specification , lines 11-18), however, the scope of the claimed invention is directed to any and all compounds that would prevent or "reduce" viral transport, or antiviral composition that would prevent general binding. The specification has limited teaching that the US11 protein of herpes simplex virus binds to kinesin of the cells to gain entry and for transport of the virus within the axon of neurons. However, the specification does not provide any teaching with respect to any

and all teguments interaction to any other motor proteins or interaction of any other virus beside HSV. Applicants own teaching is reflective of the state of the art, Applicants disclosure states that even VP16 did not bind to kinesin (see page 11, lines 19-31) and yet the scope of the invention is not reflective of such teaching, wherein absent teaching undue experimentation would be required to enable the full scope of the claimed invention. The viral transport has many mechanisms and applicants have identified only one such mechanism and yet the scope of the claims read on a general inhibition of virus transport, and compounds that would inhibit such mechanisms both in vivo and in vitro. This is not considered to be an adequate teaching, where one of ordinary skill in the art cannot practice the invention absent undue experimentation. Applicants have not taught how the methods and the product may be practiced in an in vivo milieu. No working example has been presented that would indicate " a compound" can prevent US11 protein binding to even kinesin, and yet the scope of the claims are seeking for patent protection for "antiviral composition", this is not considered adequate teaching. The scope of claimed invention reads on a protective vaccine, and no such teaching has been provided. Still further, the state of the art does not recognize that other viruses beside HSV even possess US11 tegument and yet applicants' claims are directed to viruses such as rabies or varicella-zoster to have US11 protein and bind kinesin, absent adequate teaching undue experimentation would be required, applicants can provide evidence that would indicate the US11 is present within the recited neurotropic viruses listed in the claims, the Office has not been able to locate such teaching. With regard to an antiviral composition, the specification is extremely deficient in

providing any teaching regarding such "compound(s)" that would inhibit the viral binding. Herpes Simplex Virus is a latent virus , which means its already infected the neuron cells, how does a "compound" going to prevent the binding under latently infected scenario? There is no teaching when and what "compound" is being added and where and how much of a "compound" is administered. In an unpredictable field these are not and cannot be considered routine. Applicants have general statements regarding the composition and method of prevention or reduction of infection of neurotrophic viruses utilizing compounds that would inhibit the viral binding tegument to the motor protein of cells. However with regard to an unpredictable field, this does not constitute an adequate disclosure. See Fiers v. Revel (25USPQ2d 1601 at 1606; and also decision by the Federal Circuit with regard to the enablement issues see Genentech Inc. v. Novo Nordisk A/S, 42 USPQ2d 1001-1007). For example, the CAFC stated that "It is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of an invention in order to constitute enablement." (See page 1005 of the decision). This means that the disclosure must adequately guide the art worker to determine, without undue experimentation. The applicant cannot rely on the knowledge of those skilled in the art to enable the claims without providing adequate teaching. Therefore, considering large quantity of experimentation needed, the unpredictability of the field, the state of the art, and breadth of the claims, it is concluded that undue experimentation would be required to enable the intended claim. Many of these factors have been summarized *In re Wands, 858 F.2d 731, USPQ2d 1400 (Fed. Cir. 1988).*

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a **written description** of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had **possession** of the claimed invention. In the instant disclosure, Applicants have only disclosed the association of US11 protein of Herpes Simplex Virus (HSV) with kinesin which can be utilized in an *in vitro* method only for screening compounds that would inhibit the binding between US11 and kinesin. No other tegument of any other viruses or any other motor proteins of any cells or any compound or compounds that would inhibit or reduce binding of any and all viral tegument or proteins that "mimic" such tegument or motor protein were disclosed. The specification does not set forth the metes and bounds of said elements, molecules, or mimic proteins of all sorts or any compounds that would inhibit the association of virus and motor proteins, and there is not enough information about it in literature either to guide the one of ordinary skill in the art to predict the undisclosed molecules, compounds, teguments and/or motor proteins that may be encompassed within the scope of the claimed invention as a product, and since the products are not disclosed the written description is also lacking for the method, since in order to practice the method one should be in

possession of the product. Therefore, a written description of the other claimed elements should be disclosed to overcome this rejection. See also *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism. 35 USC 112 requires inter alia that a patent specification contain a written description of the invention and the manner and process of making and using it "in such full clear and concise terms as to enable one skilled in the art ... to make and use" the invention. Case law has made it clear that the requirements for a "written description" and an "enabling disclosure" are separate. For example, where a specification contains sufficient information to enable a skilled chemist to produce a particular compound because it gives detailed information on how to produce analogous compounds but it makes no reference to the compound in question, the "written description" requirement has not been met even though the description may be enabling.

See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed, Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 12-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Roller et al (Journal of Virology, June 1992, pages 3624-3632).

The claims are directed to antiviral product capable of preventing binding a structural tegument protein and a motor protein. Roller et al taught an antibody that would bind to US11 tegument of herpes simplex virus and it would inhibit its function. The product taught by the above cited art anticipates the broad scope of the claimed invention. The product disclosed in the above cited article (see page 3625, left column, 2nd full paragraph) appears to be identical to the product claimed by the applicants. There is no indication in the claims that the antibody taught by Roller et al is not intended to be claimed. Applicants are reminded that the Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art products. Moreover, if the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Claims 12-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Sodeik et al (The Journal of cell Biology, March 1997, Vol. 136, pages 1007-1021).

The claims are directed to antiviral product capable of preventing binding a structural tegument protein and a motor protein. Sodeik et al taught "compounds" that would depolymerize micro-tubules and would reduce the infection of HSV. The products disclosed in the above cited article (see page 1016, right column, last full paragraph)

appears to be identical to the product claimed by the applicants. There is no indication in the claims that the" compounds" as taught above is/are within the scope of the claims. Applicants are reminded that the Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art products. Moreover, if the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1, 2, 4-6, 8, 9, 10, and 11 are rejected under 35 U.S.C. 102(e) as being anticipated by Kun et al (U.S. Patent No. 6,326,402 B1).

The claims are directed to a general method of preventing or reducing transport of neurotropic virus wherein a compound is introduced to prevent the binding between the structural tegument protein of the virus and motor protein. Kun et al taught a method of treating a viral infection including HSV with a compound that would inhibit the binding of micro-tubules which would lead to inhibition of binding (see the claims).

Claims 12-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Beraud et al (U.S patent No.6,346,410 B1).

The claims are directed to antiviral product capable of preventing binding a structural tegument protein and a motor protein. Beraud et al taught "compounds" that would bind kinesin and as a consequence would inhibit the infection of HSV (see Claim 2). The products disclosed in the above cited patent appears to be identical to the product claimed by the applicants. There is no indication in the claims that the "compounds" as taught above is/are within the scope of the claims. Applicants are reminded that the Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art products. Moreover, if the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Claims 12-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Beraud et al (U.S patent No.6,455,293 B1).

The claims are directed to antiviral product capable of preventing binding a structural tegument protein and a motor protein. Beraud et al taught "compounds" that would bind kinesin and as a consequence would inhibit the infection of HSV (see Claims 2, 5). The products disclosed in the above cited patent appears to be identical to the product claimed by the applicants. There is no indication in the claims that the "compounds" as taught above is/are within the scope of the claims. Applicants are reminded that the Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art products. Moreover, if the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Claims 12-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Beraud et al (U.S patent No.6,492,158 B1).

The claims are directed to antiviral product capable of preventing binding a structural tegument protein and a motor protein. Beraud et al taught "compounds" that would bind kinesin and as a consequence would inhibit the infection of HSV (see Claim

2). The products disclosed in the above cited patent appears to be identical to the product claimed by the applicants. There is no indication in the claims that the "compounds" as taught above is/are within the scope of the claims. Applicants are reminded that the Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art products. Moreover, if the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

No claims are allowed.

Conclusion

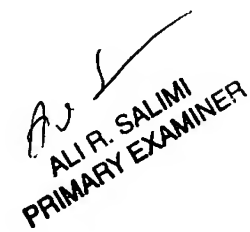
Any inquiry concerning this communication or earlier communications from the examiner should be directed to A. R. Salimi whose telephone number is (703) 305-7136. The examiner can normally be reached on Monday-Friday from 9:00 Am to 6:00 Pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is (703) 305-3014, or (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

A. R. Salimi

4/22/2003



Application No.: 10/031,492

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s)

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
- [X] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [X] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [ ] 7. Other: _____

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- [X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE